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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,679	11/14/2003	Denise Faustman	00786/428002	2917

21559 7590 10/02/2008

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EXAMINER	
JUEDES, AMY E	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
10/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/713,679	FAUSTMAN, DENISE	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-15,18,21 and 56-59* is/are pending in the application.

4a) Of the above claim(s) *58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-15,18,21,56,57 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 7/2/08 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/2/08 has been entered.

Claims 12 and 21 have been amended.
Claim 20 has been cancelled.
Claim 59 has been added.
Claims 12-15, 18, 21, and 56-59 are pending.

Claim 58 stands withdrawn from further consideration pursuant to 37 CFR 1.14209 as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 12-15, 18, 21, 56-57, and 59 are under examination.

2. Claim 57 is objected to for being dependent on cancelled claim 33.

3. The rejection of the claims under 35 U.S.C. 112 first paragraph for lack of written description for TNF-alpha agonists" or "TNF-alpha inducing substances" is withdrawn in view of Applicant's amendment to the claims. However, Applicant's arguments relevant to the new grounds of rejection will be addressed below.

4. The rejection of the claims under 35 U.S.C. 112 first paragraph for new matter for the recitation of "TNF-alpha agonists" is withdrawn in view of Applicant's amendment to the claims to recite "TNF-alpha receptor agonists".

5. Upon reconsideration, the rejection of the claims under 35 U.S.C. 112 first paragraph for lack of enablement is withdrawn. However, Applicant's arguments relevant to the new grounds of rejection will be addressed below.

6. Acknowledgment is made of applicant's claim for domestic priority under 35 U.S.C. 119(e). However, the provisional application USSN 60/426590 upon which priority is claimed fails

to provide adequate support under 35 U.S.C. 112 for claims 12-15, 18, 21, 56-57, and 59 of this application. The '590 application discloses a method for diagnosing autoimmune disease comprising treating peripheral blood cells with a compound that preferentially kills autoimmune cells, including TNF-alpha, and measuring cell death, wherein an increase in cell death compared to control cells is indicative of autoimmune disease. However, the '590 application does not disclose a method of diagnosis comprising measuring viability of "leukocytes" in a first sample relative to viability in a second sample "from a second mammal of the same species as the first mammal, wherein said second mammal does not have or is not at risk for developing said autoimmune disease". Additionally, the '590 application does not disclose a method of diagnosis comprising contacting a first and second blood sample, with a "TFN-alpha receptor agonist". Consequently, the claims have been accorded the priority of the filing date of the instant application, i.e. 11/14/2003.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 12-15, 18, 21, and 56-57 stand rejected, and claim 59 is rejected, under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

B) A method wherein a "statistically significant" decrease in leukocyte viability indicates that a mammal has autoimmune disease (Claim 12 and dependent claims 13-15, 18, 20-21 and 56-57).

Applicant indicates that support for the new limitations can be found on page 6 and in Example 2 of the specification. A review of the specification fails to reveal support for the new limitation.

Regarding B), the instant specification discloses measuring a decrease of leukocyte viability. However, the only disclosure of a "statistically significant" decrease is found in the specific examples, which involve measuring TNF-alpha induced

T cell death in patients with type I diabetes. This has a much narrower scope than the instant claims, which encompass measuring a "statistically significant" decrease in viability after contact with any TNF-alpha inducing substance or agonist in a sample from a mammal with any autoimmune disease.

Applicant's arguments filed 7/2/08 have been fully considered, but they are not persuasive.

Applicant argues that although Example 2 was performed using leukocytes from patients having type I diabetes, it is clear from the title of Example 2 that the method applies to the diagnosis of other "autoimmune diseases". Applicant further notes that Example 2 further discusses an automated method for detecting cell death in "autoimmune patients". Thus, Applicant concludes that one of skill in the art would understand that the methods of Example 2 are intended to be applicable to the diagnosis of autoimmune disease, and are not unique to the diagnosis of type I diabetes.

Even if the methods of example 2 are intended to be applicable to measuring cell death in any autoimmune disease, the example is not commensurate in scope with the instant claims. Example 2 describes several different methods of measuring cell death (for example, annexin staining, PI uptake, etc.) that can be used to measure a statistically significant decrease of TNF-alpha induce T cell death in type 1 diabetic patients. However, the instant claims encompass measuring a statistically significant decrease of leukocyte viability by any method using an TNF receptor agonist, not just using the specific methods and agonist disclosed in Example 2.

9. The following are new grounds of rejection.

10. Claims 12-15 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to demonstrate that applicant was in possession of the claimed genus of "TNF-alpha receptor agonists".

The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual

reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus.

The instant claims are drawn to a method of diagnosing autoimmune disease comprising contacting cells with a "TNF-alpha receptor agonist." This might encompass a broad range of structurally different molecules. For example, the claims encompass agonists that are antibodies, small molecules, natural or mutant ligands, peptides, etc. Furthermore, the TNF-alpha receptor agonists might function to stimulate different TNF-alpha receptors (i.e. TNFR1 or TNFR2). Thus, the claims encompass structurally different agonists that might function to stimulate structurally and functionally different receptors. The specification does not disclose a correlation between the structure and function of the claimed agonists. Furthermore, while certain classes of agonists, such as TNF receptor specific antibodies or TNF-alpha, are well known in the art, there is no art recognized correlation between the structure and function of other types of agonists, such as small molecules or peptides. For example, Hymowitz et al., Nat. Chem. Biol, 2005 teaches that due to the trimeric nature of the TNF receptor, peptide-based or small molecule based agonists that appropriately engage the receptor have been difficult to create (see page 353 in particular). Furthermore, the specification only discloses antibody agonists of TNF-alpha receptor and TNF-alpha. The disclosure of the natural ligand of TNF-alpha receptors and antibody agonists is not sufficiently representative of the broad range of structurally different agonists, including small molecules and peptides, that are encompassed by the claims. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

Applicants arguments filed 7/2/08, have been fully considered, but they are not persuasive.

Applicant argues that TNF-alpha receptor agonists are well known in the art, and the specification need not discloses what

is well-know. Applicant has submitted references as evidence of the well known nature of TNF-alpha agonists, including mutein TNF-alpha, antibodies, small molecules, and peptides.

The references demonstrate the TNF-receptor agonists that comprise antibodies and TNF-alpha muteins are well known. However, no references are provided that demonstrate the well known nature of peptide or small molecule agonists, as is encompassed by the instant claims. The references submitted by Applicant pertaining to small molecules all demonstrate the ability of certain small molecules to induce TNF-alpha production. However, these molecules are not acting as TNF-receptor agonists, since the induction of TNF-alpha is mediated through many different receptors and pathways. As taught by Hymowitz et al., 2005, small molecule agonists of the TNF-receptor are not well known in the art (see above). In fact Hymowitz et al. describe a small molecule agonist of CD40, which they describe as the first small molecule agonist of any TNF receptor superfamily member.

11. Claims 12-15, 18, 21, 56-57, and 59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for diagnosing insulin-dependent diabetes comprising contacting blood samples with TNF-alpha, and measuring a decrease in leukocyte viability of a first blood sample relative to viability in a non-autoimmune second blood sample,

does not reasonably provide enablement for:

A method for diagnosing autoimmune disease comprising contacting blood samples with TNF-alpha or a TNF-alpha receptor agonist, and measuring a decrease in leukocyte viability of a first blood sample relative to viability in a non-autoimmune second blood sample.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The instant claims are drawn to a method of diagnosing autoimmune disease, or a predisposition to said disease, comprising contacting a blood sample with TNF-alpha or a TNF-alpha receptor agonist. A diagnosis of autoimmune disease is made by detecting a preferential decrease in the viability of autoimmune leukocytes, compared to those of normal leukocytes. Thus, the asserted mechanism by which the claimed method functions is that leukocytes from patients with autoimmune disease are more susceptible to cell death. However, the instant claims encompass an overly broad method of diagnosing a wide range of different autoimmune diseases with different etiologies and pathological mechanisms. For example, the claims encompass diagnosing disease ranging from organ specific autoimmune diseases such as diabetes or multiple sclerosis, to immune deficiencies such as primary agammaglobulinemia, or infectious disease such as hepatitis, or even other diverse diseases including chronic fatigue syndrome, pulmonary fibrosis, or alopecia. It is unlikely that a single diagnosis method could be effective for such a broad range of different diseases. For example, the instant claims encompass diagnosing alopecia by detecting a decrease in leukocyte viability. However, peripheral blood lymphocytes from alopecia patients display increased resistance toward apoptosis compared to healthy controls (see Zoller et al., of record). Likewise, multiple sclerosis is associated with impaired apoptosis of PBMCs compared to controls (see Macchi et al., of record). Additionally, PBMCs from patients with rheumatoid arthritis

display reduced apoptosis compared with healthy controls (see Szodoray et al. Fig. 2 in particular, of record). Therefore, the ability to diagnose autoimmune disease by measuring a decrease in leukocyte viability is extremely unpredictable.

Additionally, even though autoimmune diseases such as type I diabetes are known to be associated with an increase in TNF-alpha mediated apoptosis (see Hayashi et al.), the instant claims encompass measuring cell viability after contact with any TNF-alpha receptor agonist. While TNF-receptor agonist antibodies are well known in the art, the claims encompass employing other agonists including peptides and small molecules. However, because of the trimeric nature of the TNF receptor, peptide-based or small molecule base agonists that appropriately engage these receptors have been difficult to create (see Hymowitz et al., Nat. Chem. Biol., 2005). Furthermore, the method encompasses using agonists that stimulate functionally different TNF receptors. There are two immunologically distinct TNF-alpha receptors (TNFR1 and TNFR2, see Tartaglia et al., of record). While TNF-alpha might induce enhanced apoptosis of leukocytes from mice predisposed to diabetes (see Hayashi et al., of record), it is known that antibody agonists of TNFR1 and TNFR2 mediate distinct activities depending on the experimental conditions. For example, anti-TNFR1 antibodies mediate apoptosis in PBMCs from healthy controls, but do not cause increased apoptosis in PBMCs from autoimmune arthritis patients (see Szodoray et al., of record). In contrast, antibodies specific for TNFR2 do not mediate cytotoxicity, but rather induce proliferation (see Tartaglia et al., Fig. 1 and Fig. 2, in particular, of record). Additionally, neither TNFR1 nor TNFR2 antibodies induce cell death in T cell blasts, although a combination of anti-TNFR1 and anti-TNFR2 antibodies is comparable to TNF-alpha in inducing T cell death (see Sarin et al., page 3717, of record). These studies demonstrate that the effect of a particular TNF-alpha receptor agonists is unpredictable, and depends on the cell subset, activation status, and specificity of the agonists (i.e. TNFR1 vs. TNFR2).

Based on the state of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the method of the claims. However, the only examples provided by the instant specification involve contacting blood samples of type I diabetic patients with TNF-alpha, followed by measuring T cell viability. This specific example demonstrates that in humans, T cells from type I

diabetics exhibit an decrease in cell viability compared to controls. The specification further demonstrates that in NOD mice predisposed to diabetes, T cells exhibit a decrease in cell viability after culture with TNF-alpha compared to controls. However, no examples are provided that demonstrate that the method can function to diagnose any other organ specific autoimmune diseases. Additionally, no examples are provided that demonstrate that autoimmune diseases can be diagnosed by contacting with TNF-alpha receptor agonists, other than TNF-alpha. Accordingly, the method as broadly claimed must be considered highly unpredictable. Given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

Applicant's arguments, filed 7/2/08 have been fully considered, but they are not persuasive.

Applicant argues that the post filing references of Konama et al. and Kuhtreiber et al. provide evidence of the enablement of the claimed invention.

The Konama et al. and Kuhtreiber et al. references demonstrate that leukocytes from subjects with type 1 diabetes exhibit decreased viability after contact with TNF-alpha compared controls. However, as noted above, the issue with regard to the lack of enablement of the instant invention relates to the unpredictability of applying those results to a the broader method of diagnosing any autoimmune disease employing any TNF-receptor agonist. The references submitted by Applicant do not provide data using leukocytes from subjects with other autoimmune disease, nor is data provided using other TNF-receptor agonists.

Applicant further argues that they have conducted further experiments with cells from patients with a variety of different autoimmune diseases, and using a variety of TNF-alpha receptor agonists, that demonstrate the enablement of the full scope of the claimed in invention.

It is noted that the data referred to by Applicant has not been submitted in declaration form, and therefore cannot be adequately considered. However, if submitted in declaration form, the data might be persuasive to overcome the rejection in part, as it pertains to a method of diagnosing autoimmune disease employing TNF-alpha. The data in Fig. S2, for example,

demonstrates that TNF-alpha causes a decrease in leukocyte viability in patients with autoimmune diseases including lupus, psoriasis, Chrohn's disease, hypothyroidism, and multiple sclerosis. However, the data would not likely be persuasive to support the enablement of a method employing TNF-receptor agonists. For example, the data in Figure 2 demonstrate that antibody agonists of TNF receptor 1 are ineffective in a method of diagnosing type 1 diabetes.

12. Claims 21 and 59 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A method of diagnosing autoimmune disease employing a "TNF-alpha receptor agonist antibody" or a "TNF-alpha receptor II agonist antibody".

Applicant indicates that support for the new limitations can be found on pages 18 and 49 of the specification.

A review of the specification fails to reveal support for the new limitations.

The specification at page 6 discloses that the method of diagnosis of the invention can employ TNF-alpha or an agonist of TNF-alpha receptor, including a human or humanized monoclonal antibody agonist. The specification further discloses using TNFR-2 agonists. Thus, the specification provides support for a method of diagnosing autoimmune disease employing a human or humanized monoclonal antibody agonists of TNF-alpha receptor or TNFR-2 receptor. However, the instant claims have a broader scope than what is disclosed by the specification and employ any antibody, not just a human or humanized monoclonal antibody. The specification at page 49 further discloses that the methods of the present invention can be used to measure the response of PBLs to monoclonal antibodies to TNF family receptors, and the specification on page 18 discloses that there are two different

TFN-alpha receptors and defective signaling through either could render autoimmune cells susceptible to apoptosis. However, said disclosure, at best, provides support for a method employing TNF-alpha receptor monoclonal antibodies, which has a narrower scope than the instant claims which encompass any antibody.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12-15, 18, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Application publication 2002/0123472 (of record).

The ‘472 publication teaches a method of diagnosing an autoimmune disease comprising treating peripheral cells of a mammal with a TNF-alpha treatment regimen and detecting cell death in the cells, wherein an increase in cell death compared to control cells indicates that the mammal has an autoimmune disease (see page 2, in particular). The '472 publication teaches that the cells can be T lymphocytes (i.e. a blood leukocyte that overexpresses receptors for TNF-alpha compared to non immune cells, for example, see page 2). The ‘472 publication also teaches that the TNF-alpha treatment regimen includes TNF-alpha agonists, such as antibodies that act on the TNF-alpha receptor (see page 3 and 6, in particular). The ‘472 publication also teaches specifically measuring a decrease in cell viability of autoimmune lymphocytes from patient with type I diabetes compared to control lymphocyte from normal human donors (i.e. those without autoimmune disease, see page 15 in particular). The ‘472 publication also teaches that in 80 control samples, no cell death was measured, while all 80 samples from type I diabetics exhibited cell death (i.e. measuring a statistically significant decrease in viability, see page 15 in particular).

Thus, the reference clearly anticipates the invention.

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by

a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 12, 15, and 18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12-15 of U.S. Patent No. 6,660,487 (of record). Although the conflicting claims are not identical, they are not patentably distinct from each other because the ‘487 patent claims a method of diagnosing autoimmune disease comprising treating peripheral cells from a mammal, including a human, with a TNF-alpha treatment regimen and detecting cell death, wherein an increase in cell death compared to control cells is indicative of autoimmune disease. The ‘487 patent also claims that the treatment regimen is TNF-alpha (i.e. a TNF-alpha receptor agonist). The ‘487 patent also claims that the cells can be T lymphocytes (i.e. a peripheral blood leukocyte that overexpresses TNF receptor compared to a non-immune cell). Additionally, the limitations of a control sample from a non-autoimmune patient and measuring a statistically significant increase in cell death (i.e. a decrease in viability) do not render the instant claims patentably distinct since it would have been routine to do so in a method of diagnosis.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E.

Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 6am - 2pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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